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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/769,744 | 01/30/2004 | Anna Helgadottir | 30847/2051-004 | 6429 |

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| EXAMINER | |
|---|---|
| GEMBEH, SHIRLEY V | |
| ART UNIT | PAPER NUMBER |
| 1614 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/769,744 | HELGADOTTIR ET AL. | |
| | Examiner | Art Unit | |
| | Shirley V. Gembeh | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *206--225* is/are pending in the application.

4a) Of the above claim(s) *207,210,214,215 and 218-224* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *206,208,209,211-213,216,217 and 225* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/22/05;2/2/07;1/17/06;7/15/05*. 5/7/07
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election of species in claims 206, 208-209, 211-213, 216-217 and 225 in the reply filed on February 17, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant specie election of BAY-X-1005 and myocardial infarction is acknowledged.

Since the compound BAY-X-1005 is elected, all the specie of the different A, B, R, Y and Z will result in the claimed specie **BAY-X-1005.** Applicant elected the FLAP genotype or halotype and monitoring the leukotriene level.

### *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on 4/22/05, 2/02/07. 01/17/06, 7/15/05 and 5/7/07 have been received and acknowledged.
The information disclosure statement filed fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. C81, C121 - C125 and C-128- C130 of the above IDS submitted references are not considered because they lack a publication date.

It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes

of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 212 and 213 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

Applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art. In the specification the mention of prodrugs is acknowledged in paragraphs 0336, 0339 and 0349 but fail to show what these prodrugs are. In particular, Applicant has not provided a description of the structure of a representative number of derivative compounds nor a description of the chemical and/or physical characteristics of a representative number of compounds nor a description of how to obtain a representative number of specific compounds.

To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that application was in possession of the claimed invention. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims **206, 208-209, 211-213 and 216-217 are** rejected under 35 U.S.C. 103(a) as being unpatentable over Isakson et al. US 6,136,839 in view of Rossoni et al. The J. of Pharm. and Exp. Ther. Vol. 276;335-341 1996 taken with Muller-Peddinghaus et al. and Gompertz et al. Chest vol.122, 289—294, 2002 and

Isakson et al. teach administering BAY-X-1005 (a 5-lipogenase inhibitor) (see col. 5, line 10) to patients with inflammatory condition, wherein the inflammatory condition is myocardial (see col.4, line 21) as in instant claim 206 and 209 and 211-212. Since the agent BAY-X-1005 is a 5-lipogenase inhibitor, administering an effective amount of BAY-X-1005 (see para.0507as evident by Khanapure et al. US 2002/0119977 A1) an inhibitor of leukotriene synthesis in vivo is obvious as the compound is a leukotriene antagonist that inhibits leukotriene synthesis as in the current claim 206. It is a known knowledge that the ability of various inhibitors of lipoxygenase (LOX) enzymes and 5-lipoxygenase-activating protein (FLAP) to induce apoptosis has implicated these pathways in the mechanism(s) of this form of cell death (inhibition/reduction) as evidence by Datta et al. (enclosed). It will be obvious that the agent will inhibit the activity of 5-lipogenase activating protein (FLAP) "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir.

1990) "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." The compound is administered orally as in claim 213 (see col. 31, lines 56-57) in a physiologically/pharmaceutically acceptable carrier is taught (see col. 31, lines 49-50). Although, the reference did not teach administering in a physiologically acceptable carrier it would be obvious to one of ordinary skill in the art to administer in a physiologically acceptable carrier as the agent is for a human as in claims 208 and 212.

Note that myocardial infarction is selecting the patient population reducing the C-reactive protein in the instant claims 206.

Rossoni et al. teach, monitoring leukotriene administering BAY-x-1005 (see abstract) wherein 20% reduction was seen with a significant protection against the increase in coronary perfusion pressure (see abstract). The Rossoni reference also teaches the BAY-X-1005 exerts a significant cardioprotection suggesting specific leukotriene inhibitors may lead to myocardial ischemia.

Although, Isakson et al. did not teach leukotriene monitoring, one of ordinary skill in the art would be motivated to monitor the leukotriene in patients with myocardial ischemia because the Rossoni et al. reference teach monitoring in rats wherein a greater protection was observed. Also since BAY-X-1005 is a potent inhibitor of 5-LOX

activating protein as discussed above one of ordinary skill in the art would expect inhibition of leukotriene.

Muller-Peddinghaus et al. teach BAY-X-1005 as an orally active inhibitor of leukotrienes (see abstract first two lines).

Gompertz et al. teach the administration (orally) of Bay-X-1005 (see abstract) monitoring the leukotriene in the patients, wherein the monitoring is from spontaneous sputum samples monitoring $LTB_4$ showed that leukotriene synthesis inhibitor BAY-X-1005 reduces $LTB_4$ in human subjects as in claims 216 and 217 (see page 290, rt. col.). As to claim 217, the reference teaches blood (see page 293 rt. col. underlined) and the knowledge of one of ordinary skill in the art know knows that blood is approximately 55% plasma, thus teaches the claimed invention. As to claim 207, the MI agent inhibits leukotriene synthesis by inhibiting the activity of lipoxygenase activating protein (FLAP) (see page 292, highlighted sec.)

One of ordinary skill in the art would have been motivated to combine the above cited art, monitor the patient serum (plasma) level by first assaying for patients with high levels of leukotriene proteins, since the reference (Rossoni et al. teach administering BAY-X-1005 lowers MI.

One of ordinary skill in the art would have been motivated to use the above teaching monitor the leucotriene level in a patient before and after the administering step because since the drug is a inhibitor of leukotriene activity, wherein the drug has shown to inhibit (lower) the 5-LOX activating protein. It is well within the knowledge of one of ordinary skill in the art to know how the inhibition is carried out by first determining the

leukotriene level before administering the drug BAY-X-1005 and after administration. These are common practice within the level of one of ordinary skill in the art (see Gometz page 292-graphs) wherein the baseline was determined and after 14 days.

Thus, the instantly claimed method using the claimed compound BAY-X-1005 would have been successful when used in the treatment of myocardial infarction as shown in the references cited.

Claim **225 is** rejected under 35 U.S.C. 103(a) as being unpatentable over Isakson et al. US 6,136,839 in view of Muller-Peddinghaus et al. Pharm. and Experimental Therapeutics (applicants prior art submission) taken with Gompertz et al. Chest vol.122, 289—294, 2002 as applied to claims **206, 208-209, 211-13 and 216-217** above further in view of Byrum et al. J. Exp. Med Vol. 185(6) 1065-1075 1997.

As to claim 225, wherein the identification of the FLAP genotype although the Byrum et al. reference did not teach explicitly the determination of Flap genotype in humans, however, the reference teaches identification of the FLAP genes in animal (mice) and showed that when the genotype is missing, reduced inflammatory response is seen (see page 1073). Even though humans are not used in the genotypying, but the knowledge that cardiovascular complication that accompanies an inflammatory response induced by leucocytes in myocardial tissue, one of ordinary skill in the art would be motivated to use BAY-X-1005 and administer to the subset of patients with a Flap genotype, and lack of FLAP and leukotrienes will result in a detectable attenuation in hypersensitive patients. Therefore one of ordinary skill in the art would be motivated

to transfer from the use of animals to humans and administer BAY-x-1005 to patients with a FLAP genotype.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

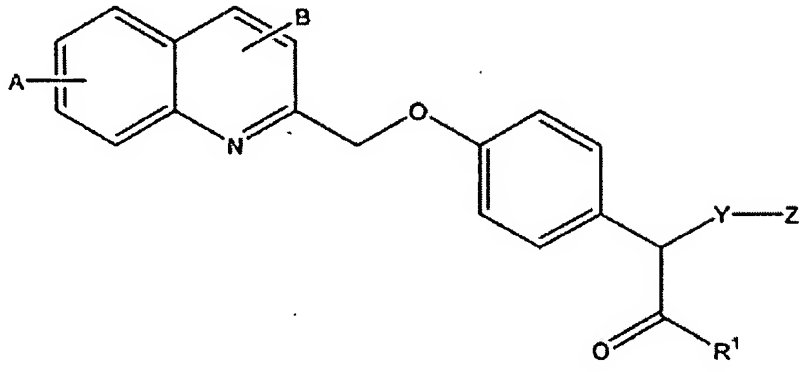
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims **206, 208-209, 211-13, 216-217 and 225** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1-7, 27-30, 32-36 and 38-41** of U.S. Patent Application No. **11270804**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

> The claims of the instant application with that of the co-pending application refer to a method of treating/prophylaxis therapy for myocardial infarction in human comprising administering a MI agent that inhibits leukotriene synthesis in vivo.

Both applications recite using the compounds such as BAY-x-1005




. See current application claims 206-210, 212-222 and 245-246 and copending application claims 1, 27-30,32-36 and 38-41.

As to the copending application claims 1-7, these claims refer to a process of identifying a nucleic acid with a genotype that correlates with race with MI in atleast one gene, therefore the instant application would have resulted in the intermediate process in screening, and since these genotypes are specific for MI the screening would have been used in the claimed process of claims 206-210, 212-222 and 245-246 in the instant application because they would have been used in producing the markers and selecting for therapy in a subject with a genotype that correlates with race wherein the MI gene, comprises nucleic acid that encodes 5-1ipoxygenase activating protein (ALOX5AP or FLAP) referred to as FLAP (see spec. of 11270804, page 7, lines 27-30)
Thus, the process is a set of precursor steps to the process of treating the MI and therefore are part of the obvious variation of the copending application claims compared to the current application claims.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Claims **206, 208-209, 211-13, 216-217 and 225** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1-10 and 12-27** of U.S. Patent Application No. **11096191**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

The claims of the instant application and that of the co-pending refer to a method of treating myocardial infarction in human comprising administering a MI agent that inhibits leukotriene synthesis in vivo.

Both applications recite using the same compound formula. See current application claims 206-210, 212-222 and 245-246 and copending application claims 1-10 and 12-27. The instant application is directed to methods of treatment (prophylactic and/or therapeutic) for certain diseases and conditions (e.g., MI, associated with FLAP or with other members of the leukotriene pathway (e.g., biosynthetic enzymes or proteins such as FLAP). Note that FLAP genotyping is elected.

The compositions recited in the co-pending claims are anticipatory of the claims in the instant application.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Claims **206, 208-209, 211-13, 216-217 and 225** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1, 4-5, 7-9, 11-12, 23-25, 37, 40 and 43-45** of U.S. Patent Application No. **10587412**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

The claims of the instant application is to a treatment of myocardial infarction wherein the compound BAY-X-1005 is used in the treatment of the instant claim sets of claims refer to a method of treating/prophylaxis therapy for myocardial infarction in human comprising administering a MI agent that inhibits leukotriene synthesis in vivo.

Both set of application claims recite using the same compositions and/or derivatives thereof. See current application claims **206, 208-209, 211-13, 216-217 and 225** and copending application claims **1, 4-5, 7-9, 11-12, 23-29, 37, 40 and 43-45**. The compositions recited in the copending application are anticipatory of the claims in the instant application.

Because they would have been used in producing the markers and selecting for therapy in a subject with a particular SEQ ID NO:1 because the claims of the instant application are identifying or selecting a human subject with a FLAP genotype (see page 7, lines 11-15 of 10/587,412) as in claims 23-29. Thus, the

process is a set of precursor steps to the process of treating the MI and therefore are part of the obvious variation of the copending application claims compared to the current application claims.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Claims **206, 208-209, 211-13, 216-217 and 225** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **206-210, 212-222, and 245-246 of** Patent Application No. **10830477**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

The claims of the co-pending application recite a method of prophylaxis or treatment for myocardial infarction by selecting the individual suffering from such and administering a leukotriene inhibitor using the compound BAY-X-1005. Similarly the claims of the instant application are to a treatment for MI in a patient administering a leukotriene inhibitor. See current application **206, 208-209, 211-13, 216-217 and 225** and copending application claims **206-210, 212-222, and 245-246**. The compositions recited in the copending claims anticipates the instant claims.

Thus the claims are obvious variant of the instant application. They both administer the same compound for the treatment of a cardiovascular condition, by a process of selecting the patient using a marker.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
4/23/07

Ardin H Marschel 5/29/07
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SUPERVISORY PATENT EXAMINER